

**REMARKS**

Reconsideration of the application is respectfully requested.

**Status of the Claims**

Claims 1-12, 17-21, 27-30, 37-49, 54-58, 63-67, 74-86, 91-95, 100-104, 111, 128-130, 138, 151, 164, and 177 have been canceled by previous amendment without prejudice or disclaimer. Accordingly, claims 13-16, 22-26, 31-36, 50-53, 59-62, 68-73, 87-90, 96-99, 105-110, 112-127, 131-137, 139-150, 152-163, 165-176, and 178-195 are pending and at issue.

Claims 13, 23, 33, 35, 50, 60, 70, 72, 87, 97, 107, and 109 have been amended for clarification. Support for these amendments is found, for example, in the claims as originally filed. Claim 106 has been amended to depend from claim 97 because claim 93 was previously canceled. Accordingly, no new matter has been added to the application.

**Obviousness-type Double Patenting and Common Ownership Rejections**

Claims 13-16, 22-26, 31-36, 50-53, 59-62, 68-73, 87-90, 96-99, 105-110, 112-127, 131-137, 139-150, 152-163, 165-176, and 178-195 stand rejected under the judicially created doctrine of obviousness-type double patenting over various claims of U.S. Patent Nos. 6,071,538; 5,714,167; 6,348,207; 6,221,367; 6,916,489; 7,005,141; 6,461,643; and 5,629,090. Applicants respectfully disagree with the rejections. Upon the finding of allowable subject matter, applicants will file a terminal disclaimer to overcome these rejections.

**Rejections Under 35 U.S.C. § 103(a)**

Claims 13-16, 22-26, 31-36, 50-53, 59-62, 68-73, 87-90, 96-99, 105-110, and 112-127, 131-137, 139-150, 152-163, 165-176, and 178-195 stand rejected as obvious over Makino, et al.

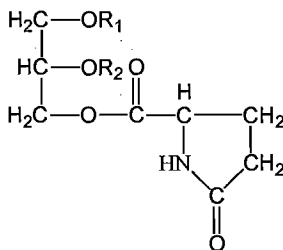
(U.S. Patent No. 4,746,675; hereafter "Makino") in view of Morishita, et al. (U.S. Patent No. 4,873,087; hereafter "Morishita").

In the most recent Office Action, the Examiner states:

With respect to the acylated amino acids, Morishita teaches compounds of formula I where A is an amino acid residue. The moieties R-CO and A read on the instant acylated amino acids because R of Morishita read on Ar moiety and CO-A is an acyl moiety. Accordingly, the claims are prima facie obvious over the above teachings.

(November 3, 2006 Office Action at pages 5-6).

The Examiner apparently does not now assert that Makino teaches compounds as penetration enhancers that read on those instantly claimed. Applicants reiterate that Makino's penetration enhancers, having the formula



with R<sub>1</sub> and R<sub>2</sub> as defined therein, do not encompass those presently claimed by Applicants.

While Morishita generally describes N-acyl amino acid derivatives or N-acyl peptide derivatives to promote absorption of an active agent, the Examiner acknowledges that Morishita does not teach subcutaneous, intranasal, or sublingual administration (November 3, 2006 Office Action at pages 3-4). Each of the presently pending claims calls for one of these three routes of administration.

However, the Examiner apparently takes the position that the routes of administration are not positively recited and do not constitute limitations on the claims at issue. The Examiner states:

Applicants' arguments with respect to the rejection of claims over Makino and Morishita have been considered but not found persuasive because instant claims recite a method "for the administration" and not "of administration." Hence the argument that Makino teaches away from the claimed invention is not persuasive. Besides, the claims do not recite any steps of administering and instead only recite providing a perturbant and active agent.

(November 3, 2006 Office Action at page 5).

Applicants have amended the claims to recite a "method ~~for~~ of subcutaneously/sublingually/intranasally administering a biologically active agent, said method comprising ...." And although Applicants submit the claims previously recited a step of administration (*see, e.g.*, step (c) of claims 13, 50, and 87), the claims have been amended to more positively recite the step of, for example, "(c) administering subcutaneously/sublingually/intranasally ~~administering~~ said supramolecular complex ...." Accordingly, the Examiner's stated basis for maintaining the rejection with regard to the routes of administration is believed to have been addressed and overcome.

Moreover, Applicants reiterate that the combined teachings of Makino and Morishita do not establish a *prima facie* case of obviousness of the present claims.

"To establish a *prima facie* case of obviousness, ... there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings." M.P.E.P. §2143; *In re Kahn*, 441 F.3d 977, 986 (Fed. Cir. 2006) (To establish a *prima facie* case of obviousness, the Examiner must "explain the reasons one of ordinary skill in the art would have

been motivated to select the references and to combine them to render the claimed invention obvious”) (*quoting In re Rouffet*, 149 F.3d 1350, 1357-59 (Fed. Cir. 1998)), *reh’g en banc denied*; *Teleflex, Inc. v. KSR Int’l Co.*, 119 Fed. Appx. 282, 285; 2005 U.S. App. LEXIS 176, \*7 (*unpub.*) (Fed. Cir. 2005), *cert. granted*.

Makino teaches penetration enhancers that are different from those disclosed in Morishita or those instantly claimed. Makino’s penetration enhancers are used for external administration. And as noted above, Makino does not teach penetration enhancers that read upon the instantly claimed perturbants.

Morishita generally describes N-acyl amino acid derivatives or N-acyl peptide derivatives to promote absorption of an active agent. Morishita does not teach subcutaneous, intranasal, or sublingual administration. Instead, Morishita teaches suppositories for vaginal or rectal delivery. Nothing in the teachings of either reference would lead one to reasonably expect that Morishita’s suppositories could be combined with Makino’s external preparations. Therefore, one of ordinary skill in the art would not be motivated to administer the N-acyl amino acid derivatives or N-acyl peptide derivatives of Morishita by any of the delivery methods taught in Makino.

Accordingly, the combination of Makino and Morishita do not fairly teach or suggest the presently pending claims.

### **CONCLUSION**

In view of the above amendments and remarks, Applicants respectfully request the withdrawal of all rejections and the allowance of all pending claims.

If there are any remaining issues that the Examiner believes could be resolved through either a Supplemental Response or an Examiner's Amendment, the Examiner is respectfully requested to contact the undersigned at the telephone number indicated below.

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Respectfully submitted,

By /Jason C. Chumney/  
Jason C. Chumney  
Registration No.: 54,781  
DARBY & DARBY P.C.  
P.O. Box 5257  
New York, New York 10150-5257  
(212) 527-7719  
(212) 527-7701 (Fax)  
Attorneys/Agents For Applicant